

# THE MERCK INDEX

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CHEMICALS, DRUGS, AND BIOLOGICALS

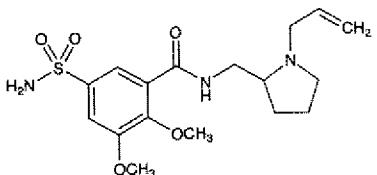
TWELFTH EDITION

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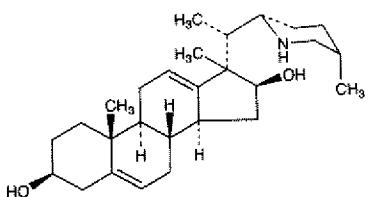
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naud, J. Macler, *ibid.* 57, 353 (1981); S. Angeli, P. Fougère, *ibid.* 58, 111 (1982).



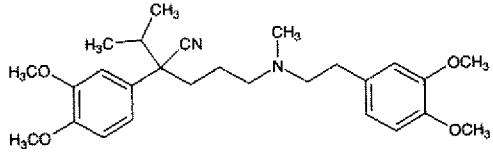
THERAP CAT: Treatment of menopausal disorders.

**10082. Veralkamine.** ( $3\beta,16\beta,17\alpha,22\alpha$ )-*17-Methyl-18-nor-16,28-secosolanida-5,12-diene-3,16-diol; 17-methyl-20 $\alpha$ -((2S,5S)-5-methyl-2-piperidyl)-18-nor-17 $\alpha$ -pregna-5,12-diene-3 $\beta$ ,16 $\beta$ -diol; (22S,25S)-12,26-epimino-17 $\beta$ -methyl-18-norcholest-5,12-diene-3 $\beta$ ,16 $\beta$ -diol; (17S,12S,25S)-22,26-epimino-18(13-17)-abeo-cholest-5,12-diene-3 $\beta$ ,16 $\beta$ -diol; veralcamine.  $C_{27}H_{42}N_2O_4$ ; mol wt 413.64. C 78.40%, H 10.48%, N 3.39%, O 7.74%. Steroidal alkaloid isolated from *Veratrum album* sp. *lobelianum* (Bergn.). Suessenguth, Liliaceae: Tomko et al., *Pharm. Zentralhalle* 99, 373 (1960); *C.A.* 55, 2013e. Structure studies: Tomko et al., *Coll. Czech. Chem. Commun.* 27, 1404 (1962). Complete structure: Tomko et al., *Tetrahedron Letters* 1967, 3907; *eidem*, *Tetrahedron* 24, 4865 (1968); Hoehne et al., *ibid.* 4875.*



Crystals from ethanol, mp 119-123° and 165-169°;  $[\alpha]_D^{24} = -84.1^\circ \pm 3$  ( $c = 0.533$  in  $CHCl_3$ ).  $N,O,O$ -Triacetate, mp 152-154°.  $[\alpha]_D^{27} = -8.0^\circ$  ( $CHCl_3$ ).  $N$ -Monooacetate, mp 191-193°.  $[\alpha]_D^{25} = -79.1^\circ$  ( $CHCl_3$ ).

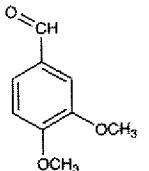
**10083. Verapamil.**  $\alpha$ -[3-[2-(3,4-Dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy- $\alpha$ -(1-methylethyl)-benzeneacetonitrile; 5-[3,4-dimethoxyphenyl]methylnicotinoyl-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile;  $\alpha$ -isopropyl- $\alpha$ -[(N-methyl-N-homoveratryl)- $\gamma$ -aminopropyl]-3,4-dimethoxyphenylacetonitrile; iproveratril; D-365.  $C_{27}H_{38}N_2O_4$ ; mol wt 454.61. C 71.34%, H 8.43%, N 6.16%, O 14.08%. Coronary vasodilator with calcium blocking activity. Prepn: Belg. pat. 615,861; Dengel, U.S. pat. 3,261,859 (1962, 1966 both to Knoll). Physical and chemical data: Appel, *Arzneimittel-Forsch.* 12, 562 (1962). Synthesis and absolute configuration of enantiomers: Ramuz, *Helv. Chim. Acta* 58, 2050 (1975). Stereospecific synthesis of enantiomers: L. J. Theodore, W. L. Nelson, *J. Org. Chem.* 52, 1309 (1987). Pharmacology: Haas, Hartfield, *ibid.* 549; Schiepper, Witzleb, *ibid.* 559. Metabolism: McIlhenny, *J. Med. Chem.* 14, 1178 (1971). HPLC determin in plasma: C. Horne et al., *Arzneimittel-Forsch.* 37, 956 (1987). Series of articles on clinical studies: *ibid.* 20, 1277-1336 (1970). Comparative study in variant angina: D. D. Waters et al., *Am. J. Cardiol.* 47, 179 (1981); in arrhythmias: B. N. Singh et al., *Drugs* 25, 125 (1983). Symposium on pharmacology and clinical efficacy in hypertension: *Am. J. Cardiol.* 57, 1D-107D (1986). Comprehensive description: Z. L. Chang, *S. Anal. Profiles Drug Subs.* 17, 643-674 (1988). Reviews: S. H. Baky, E. B. Kirsten, in *Pharmacological and Biochemical Properties of Drug Substances* vol. 3, M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1981) pp 226-261; D. J. Triggle, V. C. Swamy, *Circ. Res.* 52(2), Pt. 2, 117-128 (1983).



Viscous, pale yellow oil,  $bp_{10,0}$  243-246°.  $n_D^{25}$  1.5448. Practically insol in water. Sparingly sol in hexane; sol in benzene, ether. Freely sol in the lower alcohols, acetone, ethyl acetate, chloroform.

Hydrochloride,  $C_{27}H_{38}N_2O_4 \cdot HCl$ . *Arpamyl*, *Berkatens*, *Calan*, *Cardiagut*, *Cardibetin*, *Cordilox*, *Dignover*, *Drostekard*, *Geangin*, *Isoptin*, *Quasar*, *Securon*, *Univer*, *Vasolan*, *Veracim*, *Veramec*, *Verapin*, *Verelan*, *Verexamil*. Crystals, dec 138.5-140.5° (corr). Solv (21°): 7 g/100 g water (pH = 4.24). pH of 0.1% aq soln: 5.25. uv max: 232, 278 nm. Sparingly sol in chloroform. Sol in ethanol, isopropanol, acetone, ethyl acetate; freely sol in methanol, DMF. Solv (mg/ml): water 83, ethanol (200 proof) 26, propylene glycol 93, ethanol (190 proof) >100, methanol >100, 2-propanol 4.6, ethyl acetate 1.0, DMF >100, methylene chloride >100, hexane 0.001. pKa 8.6. LD<sub>50</sub> in rats, mice (mg/kg): 16, 8 i.v. (Baky, Kirsten). THERAP CAT: Antianginal; antiarrhythmic (class IV).

**10084. Veratraldehyde.** 3,4-Dimethoxybenzaldehyde; 3,4-dimethoxybenzenecarbonal; veratic aldehyde; protocatechualdehyde dimethyl ether.  $C_9H_{10}O_3$ ; mol wt 166.18. C 65.05%, H 6.07%, O 28.88%. Prepd by methylation of vanillin: Kostanecki, Tambor, *Ber.* 39, 4022 (1906); Buck, *Org. Syn.* 13, 102 (1933); Alt, U.S. pat. 3,007,968 (1957 to Monsanto); by oxidation of veratryl alcohol with chromium(VI) oxide-pyridine complex: Holum, *J. Org. Chem.* 26, 4814 (1961).



Needles from ether, petr ether, toluene, or carbon tetrachloride. Odor of vanilla beans; mp 42-43°;  $bp_{760}$  281°; bps<sub>1</sub> 201°;  $bp_{10}$  155°. Slightly sol in hot water; freely sol in alcohol and ether. Solns are oxidized to veratic acid under the influence of light.

**10085. Veratramine.** ( $3\beta,23\beta$ )-14,15,16,17-Tetrahydroveratraman-3,23-diol.  $C_{27}H_{38}NO_2$ ; mol wt 409.61. C 79.17%, H 9.60%, N 3.42%, O 7.81%. Secondary base from *Veratrum grandiflorum* (Maxim.) Loes. f., and from *V. viride* L., Liliaceae. Isoln and structure: Saito, *Bull. Chem. Soc. Japan* 15, 22 (1940); Jacobs, Craig, *J. Biol. Chem.* 160, 555 (1945); Jacobs, Sato, *ibid.* 181, 55 (1949); 191, 71 (1951); Tamm, Wintersteiner, *J. Am. Chem. Soc.* 74, 3842 (1952); Wintersteiner, *Festschrift Arthur Stoll* (Birkhäuser-Verlag, Basel) pp 166-176. Total synthesis: Masamune et al., *J. Am. Chem. Soc.* 89, 4521 (1967); Johnson et al., *ibid.* 4523; Masamune et al., *Tetrahedron* 27, 3369 (1971); Kutney et al., *Can. J. Chem.* 53, 1796 (1975). Stereochemistry: Sicher, Tichy, *Tetrahedron Letters* 1959(12), 6 (1959); Kataoka, *Chem. & Ind. (London)* 1961, 512; Bailey et al., *Tetrahedron Letters* 1963, 555. Revised stereochemistry: Scott et al., *ibid.* 1967, 2381; Kupchan, Suffness, *J. Am. Chem. Soc.* 90, 2730 (1968); Sprague et al., *Tetrahedron* 27, 4857 (1971). See also: Veratrum Viride.